UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,489	01/23/2001	Lisa Joanne Drewe	41577/252464	5644

23370 7590 12/27/2006

JOHN S. PRATT, ESQ
KILPATRICK STOCKTON, LLP
1100 PEACHTREE STREET
ATLANTA, GA 30309

EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/27/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/744,489	DREWE ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6,8-12,18,19 and 22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6,8-12,18,19 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action filed on October 10, 2006 has been entered.

Status of the Application

2. Currently claims 1-2, 5-6, 8-12, 18-19, 22-26 are pending. Claims 1, 18, 25 are amended. Claims 3-4, 7, 13-17, 20-21 are cancelled. The instant amendment introduces new limitations in the independent claims 1 and 18, that is, "during the amplification" which is not present in the previously examined claims. The amendment introduced new limitations as shown above and changed the scope of the independent claims. Now the scope of the independent claims is changed, accordingly the following new combination of rejections has been applied to reject newly presented claims. Applicants' arguments are fully considered and found persuasive in part for the reasons that follow. This action is made Final, necessitated by Amendment.

New Grounds of Rejections necessitated by amendment

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 6, 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vary et al. (USPN. 5,800,984) in view of Egholm et al. (WO 96/02558 A1).

Vary et al. teach a method of claims 6, for detecting the presence or absence of a target nucleic acid sequence that contains a purine rich region (triple helix-forming sequences, see col. 7, line 7-8) in the sequence in a sample comprising

(a) amplifying said target nucleic acid and so that the product of the amplification reaction includes the pruine rich region (triple helix forming sequences), wherein the resulting target is able to bind to a complementary triplex forming probe (see col. 5, line 43-55, col. 6, line 45-67, col. 7, line 7-8, col. 8, line 7-49, col. 9, line 45-54; PCR product contains purine-rich region, wherein it is capable of hybridizing with a complementary triplex forming probe);

(b) detecting the presence of triplex structures resulting from the hybridization of target sequence with the probe, wherein the detection of the presence of the triples structures indicates the presence of the target nucleic acid sequence in the sample (see col. 58-64, col. 8, line 50-56, col. 9, line 54-63).

With regard to claim 22, Vary et al. teach that the amplification reaction is a polymerase chain reaction (see col. 5, line 43-58, col. 8, line 7-10);

With regard to claim 23, Vary et al. teach that the probe is immobilized to a solid support (see col. 5, line 63-67, col. 6, line 1-14);

With regard to claim 24, Vary et al. teach the triplex structure is detected by a gel retardation method (see col. 9, line 54-67).

However, Vary did not specifically teach use of a peptide nucleic acid probe to form triplex structure.

Egholm et al. teach use of a peptide nucleic acid for diagnostic purposes, including identification of certain sites in double stranded DNA and for use in triplex forming motif (see page 6, line 19-30). Egholm et al. also teach that the PNAs provide high thermal stability, greater affinity and stable hybridization with DNA and RNA targets and resistant to degradation by enzymes (see page 3, line 15-35, page 4, line 24-29) and provide improved affinity to purine-rich regions (see page 4, line 1-36, page 17, line 13-37, page 18, line 1-26).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method for detecting the presence of a target nucleic acid in a sample as disclosed by Vary et al. et al. with a step of using a PNA probe for detecting said target nucleic acid as taught by Egholm et al. for the purpose of developing an improved detection method for enhancing the stability and specificity of the hybridization complex. One skilled in the art would be motivated to combine the method as disclosed by Vary et al. in a manner taught by Egholm et al. by the inclusion of a step of using PNA probe because Egholm et al. explicitly taught that the PNAs provide high thermal stability, greater affinity and stable hybridization with DNA and RNA targets and resistant to degradation by enzymes (see page 3, line 15-35, page 4, line 24-29) and provide improved affinity to purine-rich regions (see page 4, line 1-36, page 17, line 13-37, page 18, line 1-26). An ordinary artisan would have a reasonable expectation of success that inclusion of the step of PNA probe for detection of the target nucleic acid would result in improving the stability and specificity of the hybridization complexes with

purine-rich targets as suggested by Egholm et al. and such modification of the method would be obvious over the cited prior art in the absence of secondary considerations.

B. Claims 1, 2, 5, 8-9, 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vary et al. (USPN. 5,800,984) in view of Egholm et al. (WO 96/02558 A1) and Livak et al. (US 5,723,591).

Vary et al. teach a method of claims 1, for detecting the presence or absence of a target nucleic acid sequence in a sample comprising

(a) amplifying said target nucleic acid and introducing a purine rich region (triple helix forming region) into the target sequence during amplification, wherein the resulting target is able to bind to a complementary triplex forming probe (see col. 5, line 43-55, col. 7, line 7-8, col. 6, line 45-67, col. 8, line 7-49, col. 9, line 45-54, indicating purine rich region (triple helix forming region) is introduced into PCR product during amplification reaction, wherein it is capable of hybridizing with a complementary triplex forming probe);

(b) detecting the presence of triplex structures resulting from the hybridization of target sequence with the probe, wherein the detection of the presence of the triples structures indicates the presence of the target nucleic acid sequence in the sample (see col. 58-64, col. 8, line 50-56, col. 9, line 54-63).

With regard to claim 5, Vary et al. teach that the amplification reaction is a polymerase chain reaction (see col. 5, line 43-58, col. 8, line 7-10);

With regard to claim 8, Vary teach that the PCR primers comprise plurality of pyrimidines at the 5' end (see col. 6, line 60 indicating the triplex primer comprising plurality of pyrimidines);

With regard to claim 9, Vary et al. teach that the probe is immobilized to a solid support (see col. 5, line 63-67, col. 6, line 1-14);

With regard to claim 12, Vary et al. teach the triplex structure is detected by a gel retardation method (see col. 9, line 54-67).

However, Vary did not specifically teach use of a peptide nucleic acid probe to form triplex structure and contacting said sample with a peptide nucleic acid probe in during amplification (real-time PCR).

Egholm et al. teach use of a peptide nucleic acid for diagnostic purposes, including identification of certain sites in double stranded DNA and for use in triplex forming motif (see page 6, line 19-30). Egholm et al. teach that said peptide nucleic acid is a bis-PNA (see page 6, line 19-22). Egholm et al. also teach that the PNAs provide high thermal stability, greater affinity and stable hybridization with DNA and RNA targets and resistant to degradation by enzymes (see page 3, line 15-35, page 4, line 24-29, page 6, line 19-22) and provide improved affinity to purine-rich regions or triplex forming regions (see page 4, line 1-36, page 17, line 13-37, page 18, line 1-26).

Livak et al. teach a method for monitoring amplification and measurement of amplification products using a fluorogenic probe in the amplification reaction to monitor the fluorescence signal of the amplified product during PCR thermal cycles (see col. 8, line 55-67, col. 9, line 1-6).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method for detecting the presence of a target nucleic acid in a sample as disclosed by Vary et al. et al. with a step of using a PNA probe or a bis-PNA for

detecting said target nucleic acid as taught by Egholm et al. for the purpose of developing an improved detection method for enhancing the stability and specificity of the hybridization complex. One skilled in the art would be motivated to combine the method as disclosed by Vary et al. in a manner taught by Egholm et al. by the inclusion of a step of using PNA probe because Egholm et al. explicitly taught that the PNAs provide high thermal stability, greater affinity and stable hybridization with DNA and RNA targets and resistant to degradation by enzymes (see page 3, line 15-35, page 4, line 24-29) and provide improved affinity to triplex forming regions (see page 4, line 1-36, page 17, line 13-37, page 18, line 1-26) and modified PNAs or bis-PNAs are useful for diagnostic uses, including clamping to detect point mutations and for use in Hoogsteen type base-pairing strands in triplexing motif (see page 6, line 22-30). An ordinary artisan would have a reasonable expectation of success that inclusion of the step of PNA probe or bis-PNA for detection of the target nucleic acid would result in improving the stability and specificity of the hybridization complexes with purine-rich targets as suggested by Egholm et al. to form triplex structures. Further it is obvious to combine the teachings of Vary et al and Egholm et al. with the real-time PCR of Livak et al. because Livak et al. explicitly taught the advantage of real-time PCR using a probe hybridization during amplification, which minimizes cross-contamination or reduce false positives and provide accurate quantitation of a the target nucleic acid during PCR (see col. 2, line 21-65) and such modification of the method would be obvious over the cited prior art.

C. Claims 10-11, 18-19 rejected under 35 U.S.C. 103(a) as being unpatentable over Vary et al. (USPN. 5,800,984) in view of Egholm et al. (WO 96/02558 A1) and Livak et al. (US

5,723,591) as applied to claims 1, 2, 5, 8-9, 12, above, and further in view of Graham et al. (WO 97/05280).

Vary et al. in view of Egholm et al. and Livak et al. teach a method for detecting the presence of a target nucleic acid in a sample as discussed above in section 3B.

However, neither Vary et al. nor Egholm et al. or Livak et al. teach the use of a waveguide detector that is a surface plasmon resonance detector for detecting the presence of said target nucleic acid.

Graham et al. teach a method for detecting the presence of a target nucleic acid wherein Graham et al. teach a method comprises surface enhanced Raman scattering techniques for detecting target nucleic acids (see page 10, line 1-34). Graham et al. teach that the method comprises hybridizing target with SERS- active surface, which is in the form of a coating on a waveguide (see page 23, line 8-32).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method for detecting the presence of a target nucleic acid in a sample as disclosed by Vary et al. et al. in view of Egholm et al. and Livak et al. with a step of using waveguide detector as taught by Graham et al. for the purpose of developing a sensitive detection method for the purpose of detecting the target nucleic acid. One skilled in the art would be motivated to combine the method as disclosed by Vary et al. in view of Egholm et al. and Livak et al. in a manner taught by Graham et al. by the inclusion of a step of using a waveguide detector because Graham et al. explicitly taught that the use of the waveguide detector provides an increased sensitivity in detecting low copy number target nucleic acid s in a sample and potentially be a quick and cost-effective method for detecting target nucleic acids in a sample,

wherein the combined effect of surface enhancement and the resonance effect result in increases in sensitivity and robustness (see page 4, line 35, page 5, line 1-14, page 11, line 5-34). An ordinary artisan would have a reasonable expectation of success that inclusion of the waveguide detector for detection of the target nucleic acid would result in improving the sensitivity, robustness and cost-effective method for detecting the target nucleic acids as suggested by Graham et al. and such modification of the method would be obvious over the cited prior art.

D. Claims 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Graham et al. (WO 97/05280) in view of Egholm et al. (WO 96/02558 A1).

Graham et al. teach a kit for detecting a target nucleic acid in a sample, wherein the kit comprises a peptide nucleic probe sequence which is immobilized on a waveguide of an evanescent wave detector apparatus (see page 57, line 6-35, page 58, line 1-22, page 14, line 13-16, page 47, line 1-3, page 49, line 13-35, page 50, line 1-12), and a set of primers (see page 58, line 9-16 indicates a kit comprises other reagents for manipulating target nucleic acids, page 62, line 21-25, page 82, line 18-35, page 83, line 1-35, page 84, 1-12 indicating that the kit comprising other reagents include primers).

With regard to claim 26, Graham et al. teach that the kit evanescent wave detector apparatus, that is a surface plasmon resonance detector (see page 14, line 13-16, page 47, line 1-3, page 49, line 13-35, page 50, line 1-12).

However, Graham et al. did not specifically teach bis-peptide nucleic acid (bis-PNA).

Egholm et al. teach modified peptide nucleic acids or bis-PNA (see page 6, line 19-22). Egholm et al. also teach that modified PNAs or bis-PNAs are useful for diagnostic uses, including clamping to detect point mutations and for use in Hoogsteen type base-pairing strands

in triplexing motif (see page 6, line 22-30) and the PNAs and bis-PNA provide high thermal stability, greater affinity and stable hybridization with DNA and RNA targets and resistant to degradation by enzymes (see page 3, line 15-35, page 4, line 24-29) and provide improved affinity to purine-rich regions (triplex forming regions (see page 4, line 1-36, page 17, line 13-37, page 18, line 1-26).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the Kit composition as disclosed by Graham et al. with a bis-PNA probe as taught by Egholm et al. for the purpose of developing an improved diagnostic kit for enhancing the stability and specificity of the hybridization complex. One skilled in the art would be motivated to combine the kit as disclosed by Graham et al. in a manner taught by Egholm et al. by the inclusion of bis-PNA probe because Egholm et al. explicitly taught that the bis-PNAs modified PNA s are useful for diagnostic uses, including clamping to detect point mutations and for use in Hoogsteen type base-pairing strands in triplexing motif (see page 6, line 22-30) and the PNAs and bis-PNA provide high thermal stability, greater affinity and stable hybridization with DNA and RNA targets and resistant to degradation by enzymes (see page 3, line 15-35, page 4, line 24-29) and provide improved affinity to purine-rich regions (triplex forming regions) (see page 4, line 1-36, page 17, line 13-37, page 18, line 1-26). An ordinary artisan would have a reasonable expectation of success that inclusion of the bis- PNA probe for detection of the target nucleic acid would result in improving the stability and specificity of the hybridization complexes with triplex forming motifs of target nucleic acids as suggested by Egholm et al. and such modification of the method would be obvious over the cited prior art.

Response to arguments:

4. With regard to the rejection of claims 25-26 under 35 USC 102(b) as being anticipated by Graham et al., Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein in view of the amendment reciting bis-PNA and new grounds of rejection.

5. With regard to the rejection of claims 1, 5-6, 8-9, 12 and 22-24 under 35 USC 103(a) as being unpatentable over Vary et al. in view of Egholm et al., Applicants arguments are fully considered and found persuasive in part. The rejection is withdrawn for the claims 1-2, 5, 8-12, in view of the amendment. However the rejection is maintained for claims 6, 22-24 and the rejection is rewritten as above.

6. With regard to the rejection of claims 10-11, 18-21 under 35 USC 103(a) as being unpatentable over Vary et al. in view of Egholm et al. further in view of Graham et al., Applicants arguments and amendment are fully considered and found persuasive. The rejection is withdrawn in view of the amendment and new grounds of rejection.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Primary Examiner
Art Unit 1637

Prabha Chunduru
SURYAPRABHA CHUNDURU 12/22/06
PRIMARY EXAMINER